Patent Foramen Ovale as a Risk Factor for Altitude Decompression Illness

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Abstract
The relation between the presence of a patent foramen ovale (PFO) and the risk of decompression illness (DCI) remains controversial. PFO is a common finding in the general population, with an autopsy prevalence of about 25%. Recent review articles in the diving literature have concluded the presence of a PFO may increase the relative risk for DCI but the absolute risk remains low. In space operations, DCI is a significant concern for extravehicular activities (EVA) because of the low suit pressure (the NASA EMU-suit pressure is 4.3 psia, equivalent to about 30,000 feet). The Canadian Space Agency (through contract to DCIEM) is participating in NASA-led Prebreathe Reduction Protocol (PRP) studies to assess the safety and efficacy of reducing EVA oxygen prebreathe time. Reduction in prebreathe time is accomplished by incorporating exercise protocols during a two hour oxygen prebreathe prior to decompression to EVA suit pressure. As for NASA astronauts, DCIEM PRP subjects are screened with a trans-thoracic echocardiogram (TTE). In 48 volunteers at DCIEM screened for the PRP studies with a TTE, 14 (29%) were found to have an echo-probable PFO. In 29 altitude-exposed subjects who had a TTE, there were 5 echo-probable PFOs. None of these 5 subjects experienced DCI. Two of these subjects had a high bubble load with grade IV bubbles on precordial Doppler monitoring. In total there were four cases of Type I DCI and no Type II DCI. None of these subjects had an echo-probable PFO.

Introduction
Decompression illness (DCI) represents a significant health risk for underwater divers, caisson workers, pilots of high performance aircraft and astronauts who perform EVAs, with symptoms ranging from local joint pain (Type I), to neurological symptoms (Type II), to circulatory collapse and death. Of particular concern are the serious neurological manifestations of DCI (Type II DCI) which untreated, may lead to system collapse and death. DCI occurs as a result of the evolution of nitrogen dissolved in the body fluids and tissues when ambient pressure is decreased to the point that gas phase separation occurs. Inert gas bubbles are generally believed to form extravasculary in tissue, or intravascularly in the venous side of the circulation. Intravascular bubbles in the venous system, or venous gas emboli (VGE), circulate to the right side of the heart and eventually travel to the pulmonary circulation where they are filtered out due to the very large concentration gradient between the pulmonary capillaries and the alveoli.

Neurological complications in DCI are thought to occur as a result of the formation of gas bubbles in the tissues of the brain or spinal cord, or of arterial gas embolism (AGE). AGE may then flow to the brain and spinal cord, obstructing circulation in these tissues, causing mechanical damage, and altering biochemical and hematological balances. The presence of gas bubbles in the arterial side of the circulation is thought to occur by three possible mechanisms: 1) rupture of small airways in the lungs resulting in air embolism; 2) generation of inert gas bubbles in the arteries (de novo genesis or tribonucleation); or 3) cross-over of gas emboli from the venous to the arterial side of the circulation. Right-to-left cross-over may occur by: 1) anatomical shunts within the lung, or 2) intracardiac shunts including atrial septal defect (ASD) and patent foramen ovale (PFO).

Recently, atrial septal defects amongst divers, particularly in the form of patent foramen ovale (PFO), have been associated with the right-to-left crossover of inert gas bubbles resulting in neurological DCI (Moon *et. al.*, 1989 and Wilmhurst *et.al.*, 1989). PFO is a common finding in the general population, with an autopsy prevalence of about 25-34% (Hagen *et.al.*, 1984) and recent reports in the diving literature have concluded that the presence of a PFO increases the relative risk for DCI but the absolute risk remains low (Cross *et. el.*, 1994 and Bove, 1998).

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The relationship between Type II DCI and PFOs is less clear in the altitude environment largely due to the lack of data. Clarke & Hayes (1991) found a 16% incidence (by TTE) of PFO amongst 24 cases of Type II altitude DCI using trans-esophogeal echocardiography (TEE), suggesting that there was no significant relationship between PFO and Type II DCI. Powell *et. al.*, (1995) report a single case of a research subject who displayed a patent foramen ovale using contrast trans-cranial Doppler (TCD) and trans-thoracic echocardiography (TTE) without Valsalva maneuver. Following decompression no gas bubbles were detected in the left ventricular outflow tract or the middle cerebral artery despite numerous gas bubbles in the right heart. In addition, Pilmanis *et. al.* (1996) studied six USAF subjects who were found to have left ventricular gas bubbles at altitude in addition to high VGE scores. Of the six subjects, three had no septal defect, one had a PFO, one had a small sinus venosus, and one subject was not evaluated. Five of the cases became symptomatic at the time of AGE. The authors demonstrated that VGE can cross over to the arterial side by a number of mechanisms and suggest that altitude exposures that result in high VGE loads should be avoided by aviators.

In space operations, DCI is a significant concern for extravehicular activities (EVA) because of the low suit pressure (the NASA EMU-suit pressure is 4.3 psia, equivalent to about 30,000 feet). The Canadian Space Agency (through contract to DCIEM) is participating in NASA-led multi-centre Prebreathe Reduction Protocol (PRP) studies to assess the safety and efficacy of reducing EVA oxygen prebreathe time for International Space Station construction and maintenance EVAs. Reduction in prebreathe time is accomplished by incorporating exercise protocols during a two hour oxygen prebreathe prior to decompression to EVA suit pressure.

At DCIEM, a trans-thoracic echocardiogram and colour flow study (cardiac ultrasound) is performed on subjects as part of their medical screening. The echocardiograms are performed to detect the presence of signficant intracardiac shunts such as atrial septal defects which could put subjects at increased risk for serious decompression illness. Incidental note was made during the studies as to the possible presence of a PFO. Subjects were not excluded from the PRP study due to the echocardiographic/colour flow findings of a possible PFO. This paper presents a preliminary analysis of the incidence of PFOs amongst the DCIEM subject pool who underwent trans-thoracic echocardiography, and the occurrence of precordial bubbles and decompression illness in subjects with and without PFOs.

Methods

Volunteer subjects were recruited from DCIEM staff and from the general population, with special efforts to obtain subjects from local diving clubs, police and firefighting associations as individuals from these populations tend to more closely fit the older healthy astronaut population. In addition, many of these individuals have a general understanding of DCI and/or have experience in physiological stressful environments and in the use of breathing systems.

Prior to participating in the study, subjects underwent a trans-thoracic echocardiogram and colour flow study to exclude subjects with significant intracardiac shunts. Scans were performed by a certified ultrasound technician using a Hewlett Packard Sonos 5500. The echocardiographic study included careful colour flow interrogation of the atrial septum specifically looking for trans-septal flow. Studies included a Valsalva manoeuver. A diagnosis of "probable PFO" was made if a trans-septal colour flow pattern could be identified on several cardiac cycles.

The DCIEM altitude chamber was used to simulate the pressure changes astronauts will be exposed to within the ISS and the EVA suit. Tests involved simulating an EVA day starting 90 minutes prior to the prebreathe period up until the end of a 4 hour simulated EVA excursion to 0.3 ATA. Figure 1 displays the major events that occur throughout the EVA day.

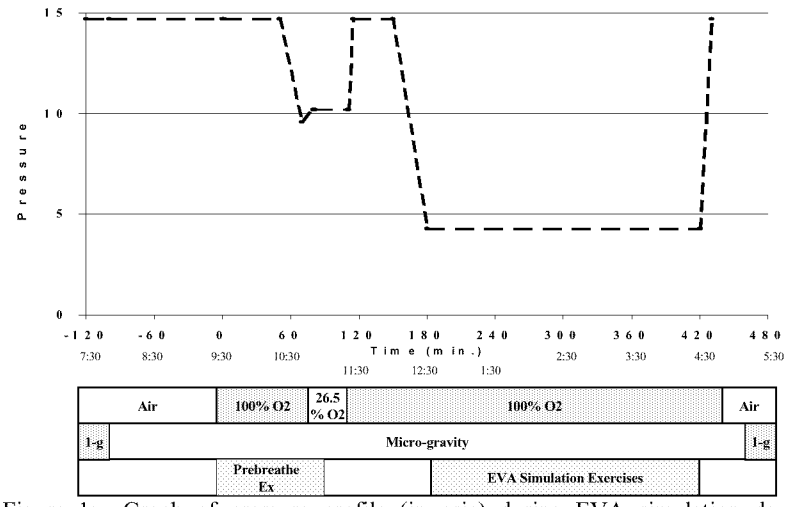

Figure 1: Graph of pressure profile (in psia) during EVA simulation day. Bottom box indicates occurrence of breathing mixtures changeovers, duration of adynamia (microgravity) and periods of exercise.

Subjects arrived at DCIEM the morning of testing and began a bedrest period for

90 minutes prior to the start of the prebreathe period. The purpose of this bedrest period (adynamia) was to simulate the weightlessness conditions of space. Subjects then donned a breathing mask and begin prebreathing 100% oxygen. Minutes after the start of prebreathe, subjects began a series of prebreathe exercises. Prebreathe exercises consisted of either high intensity short duration dual/arm leg ergometry exercises or a series of light, primarily upper body exercises performed on the cot (Figure 2).

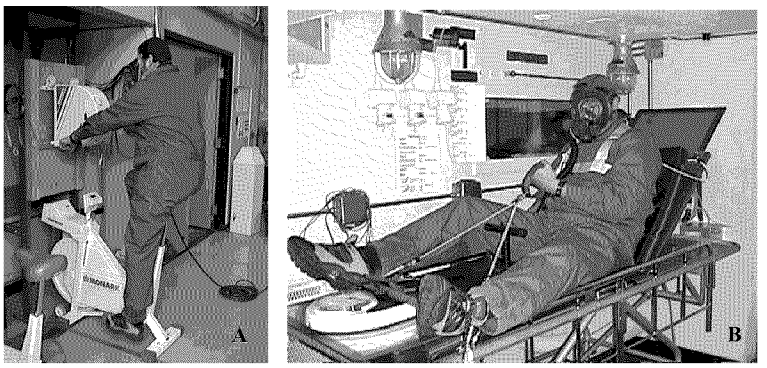

Figure 2: Photographs of two types of prebreathe exercises used to augment nitrogen washout. Figure 2a shows the dual arm/leg ergometry used in Phase II. Figure 2b shows Phase IV prebreathe exercises.

For a short period during the prebreathe exercises the pressure in the altitude chamber is reduced to 0.7 ATA (10.2 psia) and the breathing gas changed to 26.5% oxygen. This reduction in pressure and breathing gas was performed to simulate the operational environment. Following the prebreathe period, the altitude chamber pressure is reduced to 0.3 ATA (4.3 psia) to simulate the EVA environment. Throughout the EVA simulation to 0.3 ATA, subjects were monitored for symptoms of DCI. In addition, subjects were also monitored for the presence of precordial bubbles using an ultrasound unit (Model No DBM 9008, Techno Scientific Inc.) and array probe (TPI DSA7). Bubble signals were graded according to the Kisman-Masurel grading system which were then converted to the Spencer Grade Bubble Scale to allow comparison between participating laboratories (Nishi, 1993).

Results

PFO screening was not performed in the first few tests as screening was not initiated until shortly after testing began. Data presented in this paper will be is only for subjects who underwent PFO screening. In total, 48 potential subjects volunteered to participate in the study and were screened with echocardiograms (age = x ± x yrs). There were no significant cardiac abnormalities identified in any of the subjects. Fourteen of the 48 potential subjects (29.1%) had detectable PFOs (Table 1). Only 29 of the 48 volunteers participated in the chamber tests, the remaining were either unable to participate due to schedule conflicts or were eliminated from participation for medical reasons other than cardiac. Only 5 (17.2%) of the 29 participants had detectable PFOs. During altitude decompression, three of these subjects had no precordial bubbles as measured with the Doppler ultrasound unit. The remaining two subjects had detectable precordial bubbles, with one subject experiencing Grade III bubbles and the other Grade IV bubbles. None of the subjects with detectable PFOs experienced symptoms of DCI. In the total subject pool there were 4 cases of Type I DCI with no incidence of Type II DCI. Of the 4 subjects with type I DCI, none had PFOs detected by TTE.

Table 1: PFO, DCI and bubble grade incidence.

	Total Volunteers n=48	All Test Subjects n=29	Test Subjects with PFOs n=5
PFO	14 (29.1%)	5 (17.2%)	-----
DCI Type I	-----	4 (13.8%)	0
DCI Type II	-----	0	0
Bubble Grade 0		13	3
Bubble Grade I		1	0
Bubble Grade II		0	0
Bubble Grade III		6	1
Bubble Grade IV		9	1

Discussion

This study reports on PRP Phase II and Phase IV volunteers who were screened for intracardiac shunts with a trans-thoracic echocardigraphic and colour flow study. In this study, 29% of individuals who volunteered for the study and 17% of those who underwent altitude decompression were found to have a PFO based on colour flow findings of a trans-atrial septal flow pattern using TTE. None were found to have atrial septal defects or other significant cardiac abnormalities. Our reported TTE PFO incidence is higher than earlier reports and may reflect improvements in echocardiograph technology and statistical clustering. For example, autopsy results reported by Hagen *et. al.*, (1984) have revealed an incidence of 27.3% in the general population whereas studies in the early-to-mid 1990s comparing TEE and TTE have reported incidence of 11-45% using TEE and 6-9% using TTE (Siostrzonek *et. al.* 1991, Belkin *et. al.* 1994, Fischer *et. al.* 1995).

The drop in incidence from 29% in volunteers to 17% in those individuals who underwent decompression testing indicate that a larger proportion of the volunteer subject pool without PFOs went on to become test subjects than those with PFOs. The test subjects were selected from amongst the 48 volunteer based only on: 1) medical clearance by the diving medical officer, and 2) availability to participate on the scheduled test days. Medical histories resulting in exclusion from decompression testing included high blood pressure and history of complicated joint injury. No subjects were excluded from the study and none refused participation based on a positive PFO result. As a result, the lower incidence amongst test subjects is believed to be a result of statistical clustering.

Although 4 incidents of Type I DCI were diagnosed during the altitude decompressions, no subjects developed Type II DCI and none of the PFO positive subjects developed DCI. Two of the PFO positive subjects developed high levels of precordial Doppler bubbles during altitude exposure, one grade III, and the other grade IV, highlighting the fact that Type II DCI does not necessarily result from high bubble grades in the presence of a PFO.

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